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DB Name	Query	Hit Count	Set Name
USPT	osmolarity same glucose same control$ same (lactate or lactic)	2	L8
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USPT	osmolarity with glucose with control$	5	L1

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L1 94 S (OSMOLARITY) (P)(GLUCOSE)(P)(CONTROL?)
L2 0 S (CONTROLLING OSMOLARITY)(P)GLUCOSE
L3 3143 S FED-BATCH
L4 2 S L3 AND L1

FILE 'BIOSIS' ENTERED AT 15:55:06 ON 08 NOV 2001

L5 107 S (OSMOLARITY) (P)(GLUCOSE)(P)(CONTROL?)
L6 117943 S MAMMALIAN OR CHO
L7 1 S L6 AND L5
L8 109 S LACTATE (P)OSMOLARITY
L9 52 S LACTATE (P)OSMOLARITY(P)GLUCOSE
L10 1 S LACTATE (P)OSMOLARITY(P)GLUCOSE(P)(FED-BATCH)

FILE 'WPIDS' ENTERED AT 16:34:50 ON 08 NOV 2001

L11 6 S (OSMOLARITY) (P)(GLUCOSE)(P)(CONTROL?)

L5 ANSWER 34 OF 107 BIOSIS COPYRIGHT 2001 BIOSIS

AB In-situ dc electric fields were applied to remove ammonium and lactate from suspension hybridoma cultures (ATCC-CRL-1606) which used enriched media. Nutrient concentration was increased fourfold above the normal concentration of DMEM to study enhanced protein product formation in a dc electric field. In the presence of the electric field, hybridoma growth and antibody production were increased 1.5-fold (from 3.7 times 10-6 to 9.1 times 10-6 viable cells/mL) and twofold (from 170 to 505 mg IgG/L), respectively, compared with the **control**. The effective removal of ammonium and lactate and increased concentrations of the various nutrients accounted for this enhancement. The enriched media caused the overflow metabolism of **glucose**, glutamine, and various essential amino acids. The overconsumption of **glucose** also produced substantial amounts of lactate, which in turn greatly increased the medium **osmolarity**. The increase in medium **osmolarity** is believed to be one of the causes of cell death in these culture systems.

ACCESSION NUMBER: 1995:371042 BIOSIS

DOCUMENT NUMBER: PREV199598385342

TITLE: Nutrient enrichment and in-situ waste removal through electrical means for hybridoma cultures.

AUTHOR(S): Chang, Yu-Hsiang David; Grodzinsky, Alan J.; Wang, Daniel I. C. (1)

CORPORATE SOURCE: (1) Room 20A-207, MIT, 18 Vassar St., Cambridge, MA 02139 USA

SOURCE: Biotechnology and Bioengineering, (1995) Vol. 47, No. 3, pp. 319-326.
ISSN: 0006-3592.

DOCUMENT TYPE: Article

LANGUAGE: English

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L9 ANSWER 28 OF 52 BIOSIS COPYRIGHT 2001 BIOSIS

AB Adherent and suspension Baby Hamster Kidney (BHK) 21c13 cells were cultivated in a 2.5-1 stirred-tank reactor with indirect aeration. Cell concentration and viability as well as **glucose, lactate**, ammonia, and protein concentrations in the medium and intracellular and extracellular activities of the intracellular enzymes were determined off-line. The concentrations of **glucose, lactate,** ammonia, and the activity of **lactate** dehydrogenase in the culture medium were monitored on-line. The cell/cell fragment size distribution was determined by laser flow cytometer off-line. In several runs, the size distributions were ascertained on-line by a laser flow cytometer. The influence of **lactate,** ammonia, and osmotic pressure on the viability and biological parameters of the suspension cells was evaluated. In Roux flasks, **lactate** and ammonia had considerable influence on the cell properties; in stirred tank reactors, these influences were negligible up to 9.5 g l-1 **lactate** and 150 mg l-1 NH4+ ion concentrations. The influence of high **osmolarity** on the biological parameters of the cells was much less in the stirred-tank than in the Roux flasks. The adhesion of adherent cells on a surface was impeded neither by the **lactate** (up to 6 g l-1) nor by the ammonia concentration (up to 150 mg l-1). However, with increasing **osmolarity,** the fraction of the cells adhered to a surface reduced to below 5% (at 680 mOsmol l-1).

ACCESSION NUMBER: 1992:78765 BIOSIS
DOCUMENT NUMBER: BA93:47220
TITLE: INFLUENCE OF LACTATE AMMONIA AND OSMOTIC STRESS ON ADHERENT AND SUSPENSION BHK CELLS.
AUTHOR(S): WENTZ D; SCHUEGERL K
CORPORATE SOURCE: INSTITUT FUER TECHNISCHE CHEMIE, UNIVERSITAET HANNOVER, CALLINSTR. 3, D-3000 HANNOVER 1, GERMANY.
SOURCE: ENZYME MICROB TECHNOL, (1992) 14 (1), 68-75.
CODEN: EMTED2. ISSN: 0141-0229.
FILE SEGMENT: BA; OLD
LANGUAGE: English

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L7: Entry 26 of 44 File: USPT Jan 22, 1991

DOCUMENT-IDENTIFIER: US 4987154 A
TITLE: Biocompatible, stable and concentrated fluorocarbon emulsions for contrast enhancement and oxygen transport in internal animal use

ABPL:
An up to 125% fluorocarbon emulsion for use in or with animal bodies and organs thereof, maintains emulsion stability through normal sterilization procedures with selective osmotic and buffering agents, maintains the emulsion at within predetermined osmolarity levels and, when desired, free of excessive calcium precipitation, reduces in vivo and in vitro red blood cell injury, reduces adverse anemia effects, reduces viscosity and reduces the rate of oxidation, and tends to equilibrate its distribution in major body organs thereby reducing toxicity. The osmotic agents may buffer and may provide nutrient in the form of sugars. The osmotic and buffering agents can comprise, selectively, hexahydric alcohols, namely mannitol and sorbitol; certain sugars, namely glucose, mannose and fructose; along with buffering agents that will affect osmolarity including imidazole, tris(hydroxymethyl)aminomethane, sodium chloride, sodium bicarbonate, monobasic potassium phosphate, dibasic potassium phosphate, calcium chloride, magnesium sulfate, monobasic sodium phosphate, dibasic sodium phosphate or combinations of them. The emulsion may include tocopherol. A method of emulsifying the fluorocarbon includes forced flow impingement under pressure after mixing the fluorocarbon into the discontinuous phase. The fluorocarbon emulsion can be used to deliver drugs and medicines soluble in, or transportable by the emulsion.

PCPR:
This application is a continuation-in-part application of application Ser. No. 818,690, now U.S. Pat. No. 4,865,836, filed Jan. 14, 1986 in the name of David M. Long, Jr. and entitled, "Brominated Perfluorocarbon Emulsions for Internal Animal Use for Contrast Enhancement and Oxygen Transport." Priority of subject matter in this application common with subject matter in that patent is hereby claimed.

BSPR:
The present invention relates to the art of non-toxic oxygen transport and contrast enhancement agents for internal and external animal use, and more particularly to stable high concentration fluorocarbon emulsions capable of sterilization

and which are selectively free of calcium precipitation, reduce in vivo and in vitro red blood cell, or erythrocyte, injury, reduce anemia effects, and have reduced viscosity and reduced rate of oxidation or free radical damage, particularly of components of the emulsion and of contacted body tissue.

BSPR:
It has been desired, further, to provide a vehicle carrier for delivering fat or oil soluble and fluorocarbon soluble medicines through the intravascular, intraperitoneal, oral, respiratory, cerebrospinal and other internal animal body tissue or systems, including human tissue, as well as for delivering such medicines externally such as cutaneously through the skin. "Tissue" in this specification will be used to include blood.

BSPR:
Osmolarity is maintained by an osmotic agent which has benefit independent of osmolarity, such as the hexahydric alcohols, namely mannitol and sorbitol which also are used to control viscosity and stabilize particle membrane structure. Other osmotic agents, such as certain sugars, namely glucose, mannose and fructose may be used which provide nutrition. Osmolarity is also affected by buffers, which are selected from imidazole or tris(hydroxymethyl)aminomethane, which do not precipitate calcium, or may be selected from such buffering agents as sodium chloride, sodium bicarbonate, magnesium chloride, monobasic potassium phosphate, dibasic potassium phosphate, calcium chloride, magnesium sulfate, monobasic sodium phosphate and dibasic sodium phosphate. Certain biocompatible combinations of these osmotic agents provide variously or inclusively for reduction of red blood cell injury in vivo and in vitro, for reduction of viscosity, for reduction in the rate of oxidation, for nutrition and for buffering the acidity or pH level. Tocopherol, mannitol, ascorbyl palmitate and imidazole may be added or increased to further reduce the rate of oxidation of the emulsion components in vitro, and also are believed to have similar effects in vivo to reduce the rate of oxidation of the body tissue or organ to which the emulsion may be applied.

DEPR:
The emulsifying agent generally surrounds and forms a layer around the discontinuous phase creating essentially fluorocarbon particles suspended within the continuous phase. Lecithin is used frequently as the emulsifying agent, as better described in my co-pending application referenced hereinabove. Other emulsifying agents may be used with good effect, such as fluorinated surfactants, also known as fluorosurfactants and anionic surfactants. Fluorosurfactants which will provide stable emulsions include triperfluoroalkylcholate [C7F15C(.dbd.O)O]3, perfluoroalkylcholestanol [C7F15C(.dbd.O)O], perfluoroalkyloxymethylcholate, XMO-10 and fluorinated polyhydroxylated surfactants, such as, for examples, those discussed in "Design, Synthesis and Evaluation of Fluorocarbons and Surfactants for In Vivo Applications New Perfluoroalkylated Polyhydroxylated Surfactants" by J. G.

Riess, et al. Such fluorosurfactants discussed therein include a fluorophilic tail, a hydrocarbon prolongator, a junction unit comprised of an ether, an ester or an amide, and a hydrophilic head. Fluorophilic tails include, for example, C3(CF2)n, where n equals from 4 to 10. XMO-10 is a fluorinated surfactant having a formula C3F7O(CF2)3C(.dbd.O)NH(CH2)3N(.dbd.O)(CH3)2. To be an non-toxic fluorosurfactant, the fluorinated surfactant and the fluorocarbon should have an elimination rate from the animal body or organ such that the fluorocarbon and the fluorinated cosurfactant are eliminated from the body or organ before carcinosis, teratogenesis or embryotoxicity occurs. Suitable anionic surfactant which will provide a stable, non-toxic and biocompatible emulsion are polyoxyethylene-polyoxypropylene copolymers.

DEPR:
It is believed, further, that mannitol is responsible for an observed improvement in the distribution of the fluorocarbon emulsion particles among the major organs when applied within the animal body. The effects of mannitol are believed to reduce organ toxicity, which in turn is believed to largely account for the reduction of adverse anemia effects when using the emulsion.

DEPR:
The use of mannitol in the fluorocarbon emulsion, it is believed, reduces the temporary anemia effects sometimes observed during discrete time periods in animals after receiving exaggerated doses of perfluorocarbon emulsion. It is believed that the highly desired and long sought reduction in anemia effects is due to distribution equilibration of the fluorocarbon emulsion among the body organs by mannitol, and to reduction of red blood cell injury. This reduction in anemia effects has been observed in adolescent Sprague Dawley rats, as may be better seen in the following Examples I and II.

CLPR:
17. The fluorocarbon emulsion of claim 16 wherein the fluorocarbon emulsion and fluorinated surfactant have a sufficient elimination rate that the fluorocarbon emulsion and fluorinated cosurfactant are substantially eliminated from the animal body or organ before carcinosis occurs.

CLPR:
18. The fluorocarbon emulsion of claim 16 wherein the fluorocarbon emulsion and fluorinated surfactant have a sufficient elimination rate that the fluorocarbon emulsion and fluorinated cosurfactant are substantially eliminated from the animal body or organ before teratogenesis occurs.

CLPR:
19. The fluorocarbon emulsion of claim 16 wherein the fluorocarbon emulsion and fluorinated surfactant have a sufficient elimination rate that the fluorocarbon emulsion and fluorinated cosurfactant are substantially eliminated from the animal body or organ before embryotoxicity occurs.

CLPR:
32. The fluorocarbon emulsion of claim 26 including an anti-oxidant for reduction of oxidation of tissues of animal bodies and organs thereof comprising an effective amount of an anti-oxidant selected from the group consisting of ascorbyl palmitate, mannitol, tocopherol, imidazole and combinations thereof.

CLPR:
33. The fluorocarbon emulsion of claim 1 for application to tissue of animal bodies and organs thereof, further comprising mannitol and tocopherol in an effective amount for reduction of oxidation in said emulsion.

CLPR:
34. The fluorocarbon emulsion of claim 1 for application to tissue of animal bodies and organs thereof, further comprising mannitol and tocopherolan in an effective amount for reduction of oxidation in said tissue of animal bodies and organs thereof.

CLPR:
35. The fluorocarbon emulsion of claim 1 for application to tissue of animal bodies and organs thereof, further comprising mannitol in an effective amount for reduction of oxidation in said emulsion.

CLPR:
36. The fluorocarbon emulsion of claim 1 for application to tissue of animal bodies and organs thereof, further comprising mannitol in an effective amount for reduction of oxidation in said tissue of animal bodies and organs thereof.

CLPR:
37. The fluorocarbon emulsion of claim 31 for application to tissue of animal bodies and organs thereof for reduction of oxidation therein wherein said anti-oxidant group further includes ascorbic acid, salts and complexes thereof and non-calcium precipitating combinations thereof.